

by inflammatory factors expression, and histological analysis of aortic blood vessel samples was performed.

RESULTS Hypertensive subjects with VC had higher serum OPN and OPG levels compared to these without VC, and their expressions were also increased in the calcific vessels ($P < 0.05$). Interestingly, the inflammatory factors from hypertensive patients with VC were significantly increased in cultured macrophages ($P < 0.05$), and were regulated by OPN and OPG.

CONCLUSIONS These findings provided a novel insight that OPN and OPG-mediated inflammatory factors expression in macrophages were involved in the processes of VC in hypertensive patients.

GW26-e0101

IFN α 21 Correlates with ARF and non-coding RNA ANRIL Expression and the Age of CAD Onset in Han Chinese

Yan Liu,¹ Mingyu Zhang²

¹University of North Carolina at Chapel Hill, 6th floor, Burnett-Womack Building, CB# 7075, Chapel Hill, NC 27599-7075; ²Department of Cardiology, The 4th Affiliated Hospital, Harbin Medical University, Harbin, China

OBJECTIVES Multiple unbiased genome-wide wide association studies have identified a strong link between 9p21.3 locus and atherosclerotic disease risk. However, the direct mechanism accounting for the 9p21.3 CAD (Coronary Artery Disease) risk still remains poorly understood and controversial. Previous work including ours demonstrated that altered expression *INK4/ARF* locus by non-coding RNA *ANRIL* might contribute to the 9p21.3 genetic atherosclerosis susceptibility. Studies from other groups also suggested possible physical interaction among 9p21.3, *INK4/ARF* locus and type I *IFN* gene cluster. However, recent study has showed that 9p21 locus does not affect risk of coronary artery disease through direct induction of type I *IFNs*.

METHODS To investigate whether type I *IFN* is co-regulated with *INK4/ARF* and contributes to clinical onset of CAD in Han Chinese, we first examined the relationship of *IFN* subtypes with 9p21.3 variants in 170 healthy individuals in US, followed by plasma IFN α 21 measurement in 300 Han Chinese with CAD of different severity.

RESULTS We found that mRNA expression of *IFN α 21* correlated with the expression of *ARF* and *cANRIL*, as well as rs10757278 CAD risk allele. The expression of *IFN α 21* did not correlate with CAD severity quantified by coronary angiography but was associated with the age of CAD onset in Han Chinese.

CONCLUSIONS These data suggest that type I *IFNs* does not contribute to CAD severity but may play a role in the age of onset of CAD, possibly through an *ANRIL*-mediated co-regulatory mechanism with *INK4/ARF* locus.

GW26-e2506

Genetic diagnosis of familial hypercholesterolemia by targeted exome sequencing

Wenfeng Wu,¹ Lvya Wang²

¹Beijing Anzhen Hospital Affiliated with Capital Medical University, Beijing, China; ²Department of Atherosclerosis, Beijing Institute of Heart Lung and Blood Vessel Diseases, Beijing, China

OBJECTIVES The aim of this study was to combine clinical criteria and next-generation sequencing (pyrosequencing) to establish a diagnosis of familial hypercholesterolemia (FH).

METHODS A total of 39 subjects with a Dutch Lipid Clinic Network score of ≥ 8 (definite FH clinical diagnosis) were recruited from the Lipid Clinic at Anzhen Hospital, Beijing, China. Next-generation sequencing was performed in all subjects using a GenCap Custom Enrichment Kit (MyGenostics, Beijing, China), a kit that detects in 167 disease genes, relevant with blood lipids and cholic acid metabolism, including low-density lipoprotein receptor (LDLR), apolipoprotein B (APOB), proprotein convertase subtilisin/kexin type 9 (PCSK9) 3 known FH-causing genes.

RESULTS A total of 24 mutations were detected in 39 subjects. Amongst these, 19 mutations were in the LDLR gene, three in the APOB gene and two in the PCSK9 gene. We also found 151 SNPs and 69 genes relevant with blood lipids. Of these, 40 high frequency SNPs and top 10 genes were summarized. The fourth, a mutation in LDLR has not previously been reported; it was found to segregate with high cholesterol levels in the family of the proband.

CONCLUSIONS Using a combination of clinical criteria and targeted exome sequencing, we have achieved FH diagnosis with a high success rate. Furthermore, we identified a new mutation in the LDLR gene.

GW26-e2955

GPx-1^{P198L} Over Expression Showed No protection Effect on Selenium Deficiency induced Cardiac Injury in Transgenic Mice

Suqin Wang, Guang Yang, Zhongwei Liu, Yanhe Zhu, Xiaolin Niu, Dengfeng Gao
Second affiliated hospital of Xi'an Jiaotong University

OBJECTIVES Our previous study showed that decreased GPx-1 activity in KD patients was associated with the GPx-1 Pro198Leu polymorphism and Se deficiency. The purpose of this study is to further elucidate the association between different Se levels and the GPx-1^{P198L}.

METHODS GPx-1^{P198L} transgenic mice (Tg) were generated and fed by control diet (CON, 0.1-0.2mg Se/kg) or Se-deficient diet (SD, <0.02 mg Se/kg) for 12 weeks. Heart GPx-1 expression was detected by realtime RT-PCR and western blot. Echocardiographic measurements were performed to measure the cardiac function. Serum Se was analyzed by a flameless atomic absorption spectrophotometry method. Myocardial GPx activity was spectrophotometrically measured using a cellular glutathione peroxidase activity assay kit. Caspase-9 and 3 levels were detected by western blot.

RESULTS In GPx-1^{P198L} transgenic mice, heart GPx-1 expression was remarkable upregulated when compared with wide type (WT) control ($P < 0.05$), whereas, GPx-1 activity showed no difference ($P > 0.05$). Se deficiency resulted in cardiac systolic dysfunction both in WT and Tg mice and showed no difference ($P > 0.05$). Se deficiency led to myocardial fibrosis accompanied by increased expression of caspase-9 and -3 in WT mice. But in Tg mice, expression levels of caspase-9 and -3 were attenuated, whereas, myocardial fibrosis was not significantly decreased.

CONCLUSIONS Overexpression of GPx-1^{P198L} did not show evident protection against cardiac remodeling and failure. These results further documented that GPx-1^{P198L} might be a functional polymorphism which may cause functional deficiency of GPx-1.

GW26-e3821

Hypercholesterolemia abrogates the protective effect of ischemic postconditioning by induction of apoptosis and impairment of activation of reperfusion injury salvage kinase pathway

Nan Wu, Dalin Jia
Department of Cardiology, The First Affiliated Hospital of China Medical University

OBJECTIVES Ischemic postconditioning (IPOC) is an effective method to prevent myocardial ischemia reperfusion injury (MIRI), but its cardioprotection is usually blocked in the presence of hypercholesterolemia (HC) and the potential mechanism is still unknown.

METHODS In this study, we investigated the roles of reperfusion injury salvage kinase (RISK) and apoptosis-related pathways in the attenuation of cardioprotection of IPOC in the presence of HC.

RESULTS The results showed that IPOC significantly decreased the infarct size and apoptosis, improved the recovery of ischemic myocardium, but these beneficial effects were reversed by high cholesterol diet-induced HC. Moreover, we also found that HC inhibited the phosphorylation of Akt and ERK1/2 which usually activated by IPOC in normal heart, induced excessive apoptosis by down-regulating Bcl-2 and up-regulating Bax, cytochrome c, caspase 9 and caspase 3 when compared with that in normal heart.

CONCLUSIONS Taken together, our results demonstrated that the cardioprotection of IPOC was abolished by HC, which was associated with inactivation of RISK signal pathway and dysregulation of downstream apoptosis-related pathway.

GW26-e4570

Assessment of MESP1 in White Blood Cells May be Useful for Brugada Syndrome Diagnosis

Anyu Zhou,^{1,2} Ning Jiang,^{1,2} Lakir Patel,² Marco Denegri,³ Guangbin Shi,¹ An Xie,^{1,2} Hong Liu,^{1,2} Man Liu,^{1,2} Euy-Myong Jeong,^{1,2} Carlo Napolitano,³ Silvia G. Priori,³ Samuel C. Dudley, Jr.^{1,2}
¹Rhode Island Hospital, Providence, RI 02903, United States of America; ²Brown University, The Warren Alpert Medical School, Providence, RI 02903; ³Salvatore Maugeri Foundation IRCCS, Molecular Cardiology, Pavia, Italy

OBJECTIVES Brugada syndrome (BrS) is a clinical entity with high incidence of sudden cardiac death. Diagnosis of BrS solely relies on

ECG and the pathophysiological mechanism of BrS is far from clear. To find biomarkers for BrS diagnosis and to investigate possible mechanism of BrS, we conducted this study.

METHODS Twenty-five control patients, 25 BrS patients without SCN5A mutations and 20 BrS patients with SCN5A mutations were included in this study. Blood samples were collected in BD Vacutainer 9NC 0.129M (BD Biosciences). White blood cells were separated using Lympholyte-H sterile liquid. Total RNA was isolated by using Trizol® (Life Technologies) and Direct-Zol™ RNA MiniPrep Kit and was reverse transcribed with QuantiTect Reverse Transcription Kit (Qiagen). Real-time quantitative PCR (Q-PCR) analysis was performed using 7500-Fast Real-Time PCR Systems with MESP1 specific primers and probes and TaqMan® Gene Expression Master Mix (Life Technologies). MESP1 expression level was normalized by GAPDH. Differences between the groups were examined by one way ANOVA and t-tests. Results with $p < 0.05$ were considered statistically significant in all analyses.

RESULTS Among 5 cardiac specific transcription factors tested, MESP1 is one of the two expressed in white blood cells (WBC). WBC levels of MESP1 were significantly lower in BrS patients than that in normal control group (1.08 ± 0.8 in control group vs. 0.66 ± 0.38 in BrS patients without SCN5A mutation, 0.44 ± 0.42 in BrS patients with SCN5A mutation respectively, $P = 0.001$ by ANOVA analysis). T-tests revealed that the difference between control group, BrS group without SCN5A mutation and BrS group with SCN5A mutation is statistically significant ($P = 0.012$ and $P = 0.000$ respectively). Nevertheless, there was no difference detected between the two BrS groups ($P = 0.215$). The area under the Receiver Operating Characteristics analysis (ROC) curve for prediction of BrS using MESP1 levels is 0.775 (95% CI $0.668, 0.882$, asymptotic Sig.=0.000). At the optimal cutoff, the corresponding maximum sensitivity and specificity were 0.62 (95% CI: $0.47, 0.76$) and 0.88 ($0.69, 0.97$), respectively.

CONCLUSIONS MESP1 is a major cardiac specific transcription factor that expresses in white blood cells. Patients with BrS have reduced circulating MESP1. Our results suggest that assessment of circulating MESP1 may be used as a biomarker for BrS diagnosis. Our results also suggest that decreased expression of MESP1 may be one of pathophysiological mechanism of BrS.

GW26-e5401

The effect of atorvastatin on endogenous H₂S formation in red blood cell

Yonghao Lan, Mazhan, Xingshan Zhao
Beijing Jishuitan Hospital

OBJECTIVES To confirm whether can atorvastatin affect the level of H₂S in plasma through the observation on atherosclerosis model of rabbits, to assess whether atorvastatin can affect the formation of H₂S from erythrocytes. We would like to know more about the mechanism of the effect of statins on endogenous H₂S formation, for providing new ideas of variant of H₂S-directed pharmacotherapy.

METHODS We chose 36 male Japanese big ear rabbits and divide into 3 groups randomly, including normal group, high-fat-fed without medicine group (control group) and high-fat-fed with medicine group (statin group). 12 rabbits in the normal group are given normal diet. Others 24 rabbits are given high fat diet for 12 weeks. Rabbits in statin group are given atorvastatin 20mg everyday for 8 weeks (13 to 20 weeks). Determinating the level of H₂S and MPST from erythrocytes and the level of H₂S in plasma to examine mechanism of the effect of statins on endogenous H₂S formation. We measure the level of H₂S in plasma by sensitive sulphur electrode assay, measure MPST by western blotting. According to the principle of MPST enzyme catalytic reaction, we measure the level of H₂S from erythrocytes.

RESULTS The level of H₂S released from erythrocytes in high-fat-fed group was significant higher than normal group ($p < 0.05$). There were little differences in the level of H₂S in red blood cell among each group after 8 weeks ($p > 0.05$). The level of H₂S released from erythrocytes in normal group had no changes before and after observation, but it reduced remarkably in high-fat-fed without medicine group after observing 8 weeks ($p < 0.05$), it had little changes in high-fat-fed with medicine group after taking atorvastatin 8 weeks ($P > 0.05$). MPST expression in erythrocytes were resemblance among each group ($p > 0.05$). The level of H₂S in plasma in high-fat-fed without medicine group was significant lower than normal group ($p < 0.05$). It was obviously higher in high-fat-fed with medicine group than in high-fat-fed without medicine group ($p < 0.05$). The level of H₂S in plasma in high-fat-fed with medicine group was lower than normal group, but no statistical difference ($p > 0.05$).

CONCLUSIONS Atorvastatin increase net H₂S production by inhibiting its mitochondrial oxidation and reducing CoQ concentration. However atorvastatin can not affect the formation of endogenous H₂S released from erythrocytes depended mainly on MPST pathway. Therefore atorvastatin can not affect endogenous H₂S formation in red blood cell.

GW26-e5440

Elevated glycated albumin and reduced endogenous secretory receptor for advanced glycation endproducts levels in serum predict major adverse cardio-cerebral events in patients with type 2 diabetes and stable coronary artery disease

Ying Shen, Zhenkun Yang, Weifeng Shen, Hua Meng, Ruiyan Zhang, Qi Zhang, Lin Lu
Department of Cardiology, Rui Jin Hospital, Institute of Cardiovascular Diseases, Shanghai Jiaotong University School of Medicine, Shanghai 200025, PR

OBJECTIVES Glycated albumin (GA) and the endogenous secretory receptor for advanced glycation endproducts (esRAGE) may modulate risk related to atherosclerosis. We tested the hypothesis that elevated GA and reduced esRAGE in serum are associated with adverse clinical outcomes in patients with type 2 diabetes and stable coronary artery disease (CAD).

METHODS We determined GA and esRAGE serum levels in 576 consecutive patients with type 2 diabetes and stable CAD undergoing sirolimus-eluting stent (SES)-PCI. The primary endpoint was the incidence of major adverse cardio-cerebral events (MACCE) including cardiac death, non-fatal myocardial infarction, and non-fatal stroke during a 2-year follow-up. The secondary endpoint was the occurrence of clinically driven repeat revascularization during a 2-year follow-up. The prognostic value of GA and esRAGE was determined with the Cox-proportional hazards model after adjustment for covariates.

RESULTS A total 40 patients (6.9%) experienced MACCE, and 108 (18.8%) patients underwent repeat coronary revascularization during the follow-up. Serum GA levels correlated positively (both $p < 0.001$), while serum esRAGE levels negatively (both $p < 0.05$), with the primary and secondary endpoints, respectively. Serum GA (HR=1.220, 95% CI 1.160-1.283; HR=1.152, 95% CI 1.113-1.191, respectively; both $p < 0.001$) and esRAGE (HR=0.597, 95% CI 0.407-0.874; HR=0.751, 95% CI 0.613-0.919, respectively; both $p < 0.01$) levels remained independent predictors of the primary and secondary endpoints after adjustment for possible confounders.

CONCLUSIONS Serum GA and esRAGE are novel predictors of long-term clinical outcomes in patients with type 2 diabetes and stable CAD. Increased serum GA and decreased esRAGE are associated with a poor prognosis in such patients.

GW26-e0740

Safety and Efficacy of IntraCoronary Hypoxia-preconditioned Bone Marrow MonoNuclear Cell Administration for Acute Myocardial Infarction Patients: The CHINA-AMI Randomized Controlled Trial

Xinyang Hu,¹ Xin Huang,^{1,2} Qian Yang,^{1,2,3} Lihua Wang,⁴ Jianzhong Sun,⁴ Hongwei Zhan,⁵ Jianjing Lin,^{1,2} Zhaoxia Pu,³ Jun Jiang,^{1,2} Yong Sun,^{1,2} Meixiang Xiang,^{1,2} Xianbao Liu,^{1,2} Xiaojie Xie,^{1,2} Xia Yu,^{1,2} Zexin Chen²

¹Department of Cardiology, Second Affiliated Hospital, College of Medicine, Zhejiang University, Hangzhou, PR China; ²Cardiovascular Key Laboratory of Zhejiang Province, Hangzhou, PR China; ³Department of ultrasonography, Second Affiliated Hospital, College of Medicine, Zhejiang University, Hangzhou, PR China; ⁴Department of radiology, Second Affiliated Hospital, College of Medicine, Zhejiang University, Hangzhou, PR China; ⁵Department of Nuclear Medicine, Second Affiliated Hospital, College of Medicine, Zhejiang University, Hangzhou, PR China

OBJECTIVES Pre-clinical studies have shown that hypoxia preconditioning can enhance stem cell therapeutic potential for myocardial repair. We sought to investigate the safety and feasibility of intracoronary administration of hypoxia-preconditioned bone marrow cells (HP-BMCs) for acute ST segment elevation myocardial infarction (STEMI).

METHODS We randomized 22 patients with acute STEMI to receive intracoronary administration of normoxia BMCs (N-BMCs) (n=11) or HP-BMCs (n=11) following successful revascularization. Another 14 patients were recruited as the control (n=14).